

**AMENDMENTS TO THE CLAIMS:**

Please amend Claims 1 – 31 as follows:

1. (Original) A dispersible and orodispersible solid pharmaceutical composition having the form of particles with a size lower than 710  $\mu\text{m}$ , containing the metformin active ingredient, characterized in that it comprises:

a) from 65% to 90% in weight of the metformin active ingredient, optionally under the form of a salt, or a combination of the metformin active ingredient with a hypoglycemic active ingredient;

b) from 0.5 to 4% in weight of a binding agent or a combination of binding agents;

c) from 1% to 12% in weight of a disintegrating agent or a combination of disintegrating agents;

d) from 0% to 10% in weight of a diluting agent or a combination of diluting agents;

e) from 0.05% to 3% in weight of a sweetening agent or a combination of sweetening agents; and

f) one or more additional excipients,

the weight percentages being expressed based on the total weight of said composition.

2. (Original) A composition according to claim 1, characterized in that it also comprises from 0.01% to 6% in weight of a flavouring agent, or a combination of flavouring agents.

3. (Currently Amended) A composition according to ~~any one of claims 1 and 2~~ claim 1, characterized in that the binding agent(s) is (are) selected amongst polyvinylpyrrolidone, sodium carboxymethylcellulose, alginic acid, hydroxypropylmethylcellulose and polyethylene oxide.

4. (Currently Amended) A composition according to ~~any one of claims 1 to 3~~ claim 1, characterized in that the disintegrating agent(s) is (are) selected amongst sodium croscarmellose, cross-linked polyvinylpyrrolidone, sodium starch glycolate, wheat or corn starch and pre-gelatinized starch.

5. (Currently Amended) A composition according to ~~any one of claims 1 to 4~~ claim 1, characterized in that the diluting agent(s) is (are) selected amongst lactose, mannitol, cellulose, microcrystalline cellulose and calcium carbonate.

6. (Currently Amended) A composition according to ~~any one of claims 1 to 5~~ claim 1, characterized in that the sweetening agent(s) is (are) selected amongst gluconate, aspartame, cyclamate, sodium saccharinate, xylitol and maltitol.

7. (Currently Amended) A composition according to ~~any one of claims 4 to 6~~ claim 2, characterized in that the flavouring agent(s) is (are) selected amongst fruit flavour, mint flavour, anise flavour, honey flavour, vanilla flavour, tea flavour, and verbena flavour.

8. (Currently Amended) A composition according to ~~any one of claims 4 to 7~~ claim 1, characterized in that the metformin active ingredient has the form of a salt selected amongst the phosphate, sulfate, hydrochloride, salicylate, maleate, benzoate, ethanedisulfonate, fumarate, succinate, chlorophenoxyacetate, embonate and glycolate salts.

9. (Currently Amended) A composition according to ~~any one of claims 4 to 8~~ claim 1, characterized in that the hypoglycemic active ingredient, when present, is selected amongst glicazide, glipizide, chlorpropamid, glimepiride, glibenclamide, and derivatives thereof.

10. (Currently Amended) A composition according to ~~any one of claims 4 to 8~~ claim 1 characterized in that it comprises, additionally, a PPAR Gamma agonist (peroxisome proliferator-activated receptor gamma) or Glitazone, selected amongst rosiglitazone, pioglitazone, and balaglitazone and derivatives thereof.

11. (Currently Amended) A composition according to ~~any one of claims 4 to 8~~ claim 1 characterized in that it comprises, additionally, a PPAR Gamma and

Alpha agonist or Glitazar selected amongst terapglitazar, muraglitazar, and ragaglitazar and derivatives thereof.

12. (Currently Amended) A composition according to ~~any one of claims 1 to 8~~ claim 1 characterized in that it comprises, additionally, a hypocholesterol agent of fibrate type, such as fenobibrate and derivatives thereof.

13. (Currently Amended) A composition according to ~~any one of claims 1 to 8~~ claim 1 characterized in that it comprises, additionally, an active ingredient selected amongst a dipeptidyl peptidase inhibitor (DPPIV).

14. (Currently Amended) A composition according to ~~any one of claims 1 to 8~~ claim 1 characterized in that it comprises, additionally, acarbose or derivative thereof.

15. (Currently Amended) A composition according to ~~any one of claims 1 to 14~~ claim 1, characterized in that it comprises:

a) from 65% to 80% in weight of the metformin active ingredient, optionally under the form of a salt, or a combination of the metformin active ingredient with a hypoglycemic active ingredient;

b) from 0.5 to 4% in weight of a water-soluble polyvinylpyrrolidone with a molecular ranging from 44,000 to 54,000;

c) from 1% to 10% in weight of a water-insoluble cross-linked polyvinylpyrrolidone;

d) from 0.5% to 10% in weight of a diluting agent or a combination of diluting agents;

e) from 0.05% to 3% in weight of a sweetening agent or a combination of sweetening agents; and

f) one or more additional excipients,

the weight percentages being expressed based on the total weight of said composition.

16. (Currently Amended) A composition according to ~~any one of claims 1 to 15~~ claim 1, characterized in that it ~~consists in~~ comprises (i) an internal core comprising the active ingredient or the combination of active ingredients, in association with one or more excipients and (ii) an external layer comprising the sweetening agent.

17. (Original) A composition according to claim 16, characterized in that the internal core accounts for 75% to 85% in weight and in that the external layer accounts for 15% to 25% in weight, based on the total weight of the composition.

18. (Currently Amended) A composition according to any one of claims 16 or 17, ~~characterized in that it consists respectively in~~ wherein:

(i) ~~an~~ the internal core ~~comprising~~ comprising:

a) from 65% to 80% in weight of the metformin active ingredient, optionally under the form of a salt or a combination of the metformin active ingredient with a hypoglycemic active ingredient, and

b) from 0.5% to 4% in weight of a binding agent or a combination of binding agents;

and

(ii) ~~an~~ the external non-film-coated layer is non-film coated and comprises comprising :

a) from 0% to 10% in weight of a diluting agent or a combination of diluting agents;

b) from 1% to 10% in weight of a disintegrating agent or a combination of disintegrating agents; and

c) from 0.05% to 3% in weight of a sweetening agent or a combination of sweetening agents;

the weight percentages being expressed based on the total weight of said composition.

19. (Original) A composition according to claim 18, characterized in that the binding agent is a water-soluble polyvinylpyrrolidone with a molecular weight ranging from 44,000 to 54,000.

20. (Currently Amended) A composition according to ~~any one of claims 18 or 19~~ claim 18, characterized in that the disintegrating agent is a water-insoluble cross-linked polyvinylpyrrolidone.

21. (Currently Amended) A composition according to ~~any one of claims 18 to 20~~, characterized in that it comprises claim 18, wherein:

(i) ~~an~~ the internal core ~~comprising~~ comprises:

a) from 76% to 77% in weight of the metformin active ingredient, optionally under the form of a salt or a combination of the metformin active ingredient with a hypoglycemic active ingredient, and

b) from 2.5% to 3.5% in weight of a water-soluble polyvinylpyrrolidone with a molecular weight ranging from 44,000 to 54,000;

and

(ii) ~~an~~ the external non film-coated layer ~~comprising~~ comprises:

a) from 6.5% to 7.5% in weight of a diluting agent or a combination of diluting agents;

b) from 4.5% to 5.5% in weight of a water-insoluble cross-linked polyvinylpyrrolidone; and

c) from 0.5% to 2.5% in weight of a sweetening agent or a combination of sweetening agents;

the weight percentages being expressed based on the total weight of said composition.

22. (Currently Amended) A composition according to ~~any one of claims 1 to 24~~ claim 1, characterized in that it consists in:

(i) an internal core comprising:

a) 76,92% in weight of the metformin hydrochloride active ingredient, and

b) 3.08% in weight of a water-soluble polyvinylpyrrolidone with a molecular weight ranging from 44,000 to 54,000;

and

(ii) an external non film-coated layer comprising:

a) 7% in weight of a diluting agent or of a combination of diluting agents;

b) 5% in weight of a water-insoluble cross-linked polyvinylpyrrolidone;

c) 2% in weight of a sweetening agent or a combination of sweetening agents;

d) 5% in weight of a flavouring agent or a combination of flavouring agents;

and

e) 1% in weight of a preservative;

the weight percentages being expressed based on the total weight of said composition.

23. (Currently Amended) A hydrodispersible non film-coated pharmaceutical tablet, characterized in that it consists in a composition according to ~~any one of claims 1 to 22~~ claim 1.



24. (Original) A tablet according to claim 23, which pharmacokinetic profile established from two tablets, each dosed at 500 mg, is characterized by an area under the plasma concentration curve measured *in vivo* (AUC) ranging from 10000 ng.h/ml to 16250 ng.h/ml and preferably of about 12500 ng.h/ml

25. (Original) A tablet according to claim 23 or 24, which pharmacokinetic profile established from two tablets, each dosed at 500 mg, is characterized by a maximum plasma concentration value ( $C_{max}$ ) ranging from 1600 ng/ml to 2600 ng/ml and preferably of about 2000 ng/ml.

26. (Currently Amended) A tablet according to any one of claims 23 to ~~25~~ or 24, which pharmacokinetic profile established from two tablets, each dosed at 500 mg, is characterized by a  $T_{max}$  value ranging from 2h and 3.25h and preferably of about 2.5h

27. (Currently Amended) A tablet according to ~~any one of claims 23 to 26~~ claim 23, dosed at 500 mg in metformine chlorhydrate, giving results that can be extrapolated to the compositions of the same type and comprising lower doses in metformine chlorhydrate, metformine chlorhydrate absorption in human beings, being linear from 0 to 1000 mg.

28. (Currently Amended) A tablet according to ~~any one of claims 23 to 26~~ claim 23, dosed at 500 mg, releasing between 50% and 100% of the active

ingredient dose and preferably at least 80% of the metformine chlorhydrate dose in 5 minutes in a physiological buffer medium pH 6,8 at 37°C.

29. (Currently Amended) A method for preparing a hydrodispersible non film-coated pharmaceutical tablet ~~according to any one of claim 23 to 28,~~ characterized in that it comprises the following steps of:

a) ~~preparing the core (i) as defined in claim 16~~ (i) an internal core comprising a dispersible and orodispersible solid pharmaceutical composition having the form of particles with a size lower than 710 µm, containing the metformin active ingredient, the composition comprising:

1) from 65% to 90% in weight of the metformin active ingredient, optionally under the form of a salt, or a combination of the metformin active ingredient with a hypoglycemic active ingredient;

2) from 0.5 to 4% in weight of a binding agent or a combination of binding agents;

3) from 1% to 12% in weight of a disintegrating agent or a combination of disintegrating agents;

4) from 0% to 10% in weight of a diluting agent or a combination of diluting agents; and

5) one or more additional excipients.

through wet granulation of a mixture of metformin appropriate amounts, optionally under the form of a salt or a combination of the metformin active ingredient with a hypoglycemic active ingredient, and a binding agent;

b) drying the granules obtained in step a);

c) adding to the granules obtained in step b) the mixture of excipients forming ~~the external layer (ii) such as defined in claim 16;~~ (ii) an external layer comprising from 0.05% to 3% in weight of a sweetening agent or a combination of sweetening agents; the weight percentages being expressed based on the total weight of said composition; and

d) performing a compression of the granules obtained in step c).

30. (Currently Amended) A method for preparing a hydrodispersible non film-coated pharmaceutical tablet ~~according to any one of claims 23 to 28,~~ characterized in that it comprises the following steps of:

a) preparing (i) an internal core comprising a dispersible and orodispersible solid pharmaceutical composition having the form of particles with a size lower than 710  $\mu\text{m}$ , containing the metformin active ingredient, the composition comprising:

1) from 65% to 90% in weight of the metformin active ingredient, optionally under the form of a salt, or a combination of the metformin active ingredient with a hypoglycemic active ingredient;

2) from 0.5 to 4% in weight of a binding agent or a combination of binding agents;

3) from 1% to 12% in weight of a disintegrating agent or a combination of disintegrating agents;

4) from 0% to 10% in weight of a diluting agent or a combination of diluting agents; and

5) one or more additional excipients,

through dry granulation of a mixture of metformin appropriate amounts, optionally under the form of a salt or a combination of the metformin active ingredient with a hypoglycemic active ingredient, and a binding agent;

b) compacting the dry granules obtained in step a);

c) adding to the granules obtained in step b) the mixture of excipients forming ~~the external layer (ii) such as defined in claim 16-~~ (ii) an external layer comprising from 0.05% to 3% in weight of a sweetening agent or a combination of sweetening agents; the weight percentages being expressed based on the total weight of said composition; and

d) performing a compression of the granules obtained in step c).

31. (Currently Amended) A method for preparing a hydrodispersible non film-coated pharmaceutical tablet ~~according to any one of claims 23 to 28,~~ characterized in that it comprises the following steps of:

a) preparing a mixture of (i) an internal core comprising a dispersible and orodispersible solid pharmaceutical composition having the form of particles with a size lower than 710 µm, containing the metformin active ingredient, the composition comprising:

1) from 65% to 90% in weight of the metformin active ingredient, optionally under the form of a salt, or a combination of the metformin active ingredient with a hypoglycemic active ingredient;

2) from 0.5 to 4% in weight of a binding agent or a combination of binding agents;

3) from 1% to 12% in weight of a disintegrating agent or a combination of disintegrating agents;

4) from 0% to 10% in weight of a diluting agent or a combination of diluting agents; and

5) one or more additional excipients,

through dry granulation of a mixture of the metformin appropriate amounts, optionally under the form of a salt or a combination of the metformin active ingredient with a hypoglycaemic active ingredient, and the binding agent;

b) adding to the granules obtained in step a) the excipient mixture forming ~~the external layer (ii) such as defined in claim 16~~ (ii) an external layer comprising from 0.05% to 3% in weight of a sweetening agent or a combination of sweetening agents; the weight percentages being expressed based on the total weight of said composition; and

c) performing a compression of the granules obtained in step b).